REMARKS

Claims 1-24 are presently pending in the application. Claims 1, 2 and 20 are amended, and claim 24 is added, by this response.

Claims 13-23 were objected to as lacking proper antecedent basis. Office Action, page 3. The Patent Office asserts that the "generic method steps recited in claim 13 *in sequence*, cannot be found in the specification as filed." *Id.* Applicants respectfully direct the examiner's attention to the paragraph spanning pages 4 and 5 of the specification, where the process steps of claim 13 are set forth in the precise order recited in the claims. The process steps are described in further detail, in the order recited in claim 13, starting with the fifth full paragraph on page 6 of the specification, through the second full paragraph on page 8. Example 4 also describes the process, with the steps in the order recited in claim 13. Applicants respectfully request withdrawal of this objection in view of this disclosure.

Claim 20 was rejected under 35 USC § 112, second paragraph, as being indefinite in its recitation of "said prokaryotic host," a term lacking antecedent basis in claim 13, from which it depends. Office Action, page 4. New claim 24 has been added, which recites the process of claim 13 wherein the crude preparation is obtained from a prokaryotic host cell expressing the

Claims 1-10 were rejected under 35 USC § 102(b) as being anticipated by Bochner et al., US Patent 4,680,262. The Patent Office states that Bochner discloses a method for the preparation of human Growth Hormone (hGH) from transformed E. coli cells, comprising culturing a transformed E. coli culture in LB medium and tetracycline, after which steam is immediately injected into the fermenter jacket, raising the temperature rapidly. Office Action at pages 4-5. The Patent asserts that "[d]uring this time hGH is secreted into the *periplasm* of the transformed E. coli host cells ... as required by the instant independent claims," and that "the reference discusses extraction of the polypeptide of interest by osmotic shock." Office Action, page 5.

By the present amendments, claim 1 has been clarified to state that the osmotic shock is induced while the cells are still in the fermentation medium (as stated in the original claims, albeit less clearly: "applying an osmotic shock to the host cells *contained in the fermentation medium*"). This is not the method of Bochner. Bochner in fact states that osmotic shock is a "disadvantageous" method, because it requires " first treatment of viable cells with a solution of high tonicity and second with a cold water wash of low tonicity to release periplastic proteins." Col. 2, lines 45-50. Furthermore, unlike the presently claimed method of apply the osmotic shock directly to cells in fermentation medium, the methods of Bochner involve the steps of

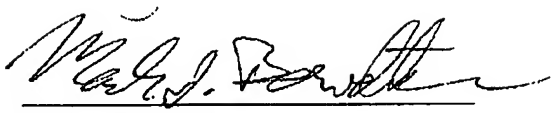
forming a cell paste, followed by resuspension buffer (col. 5, lines 22-27), precisely the steps that the present invention is directed to avoiding (see, e.g., the fourth paragraph of page 1 through the first paragraph of page 2 of the present specification). Furthermore, Bochner particularly states that by the disclosed methods "[e]ukaryotic periplasmic proteins may be obtained in higher specific activity, i.e., purity, than is attained with osmotic shock methods, and treatment with a hypertonic agent such as 20 percent sucrose is not required." Col. 5, 29-33. Though Bochner does then seemingly reverse tack and make the general statement that "any method for causing the outer membrane of the cell to become permeable to the periplasmic proteins can be used with *killed cells*" (col. 5, 33-36), it is clear that the reference to osmotic shock and sucrose is in the context of *inferior* methods the disclosed process was intended to improve upon. At most, Bochner suggests the option of using osmotic shock to permeablize killed cells resuspended in buffer, though it is made clear this is considered an unnecessary and in fact undesirable step, but provides no disclosure of applying an osmotic shock to cells in their fermentation medium, as provided by the present claims. Bochner, in fact, characterizes this as the disadvantageous approach that the disclosed method was meant to improve over. In sum, Bochner does not disclose each and every limitation of claims 1-10, arranged as in those claims. Bochner does not, therefore, anticipate the claims 1-10. Applicants respectfully request that this rejection be reconsidered and withdrawn.

Claims 1-12 have been rejected under 35 USC § 102(e) as being anticipated by Kwon et al, US Pub. 2004/0151695. According to the Patent Office, Kwon discloses each element of the claims. Office Action, pages 5-6. As with Bochner, however, Kwon does not in fact disclose the method of claims 1-12, i.e., Kwon lacks a disclosure of applying an osmotic shock to cells in their fermentation medium. Like Bochner, Kwon discloses the standard recovery method comprised of centrifuging cells to remove them from the fermentation medium, followed by resuspension and osmotic shock in the resuspension buffer. See, Examples 3 & 4. As explained above in distinguishing the Bochner reference, this is not the method of the present claims, and are in fact the very kind of process steps that is avoided by the invention of claims 1-12. See, Specification, page 1, fourth par. - page 2, second par.). Because Kwon does not disclose each element of claims 1-12, as arranged in the claims, it cannot anticipate. Applicants respectfully request that this rejection be reconsidered and withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully submit that the present claims 1-24 are in condition for allowance, and free of the prior art. Favorable action on the claims is earnestly solicited.

Respectfully submitted,



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